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LUNG CANCER AMONG CHINESE WOMEN

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A case-control study involving interviews with 672 female lung cancer patients and 735 population-based controls was conducted to investigate the high rates of lung cancer, notably adenocarcinoma, among women in Shanghai. Cigarette smoking was a strong risk factor, but accounted for only about one-fourth of all newly diagnosed cases of lung cancer. Most patients, particularly with adenocarcinoma, were life-long non-smokers. The risks of lung cancer were higher among women reporting tuberculosis and other pre-existing lung diseases. Hormonal factors were suggested by an increased risk associated with late menopause and by a gradient in the risk of adenocarcinoma with decreasing menstrual cycle length, with a 3-fold excess among women who had shorter cycles. Perhaps most intriguing were associations found between lung cancer and measures of exposure to cooking oil vapors. Risks increased with the numbers of meals cooked by either stir frying, deep frying or boiling; with the frequency of smokiness during cooking; and with the frequency of eye irritation during cooking. Use of rapeseed oil, whose volatiles following high-temperature cooking may be mutagenic, was also reported more often by the cancer patients. The findings thus confirm that factors other than smoking are responsible for the high risk of lung cancer among Chinese women and provide clues for further research, including the assessment of cooking practices.

The age-adjusted annual lung cancer incidence rate among females in Shanghai during the 1970's and 1980's has been about 20 per 100,000 population, one of the highest rates in China and in the world (National Cancer Control Office, 1980; Gao, 1982; Waterhouse *et al.*, 1982; Shanghai Cancer Registry, 1983). Elevated lung cancer death rates have also been observed among Chinese women in other parts of the world, including Hong Kong (Kung *et al.*, 1984; Koo *et al.*, 1985), Singapore (MacLennan *et al.*, 1977) and the United States (Fraumeni and Mason, 1974; Hinds *et al.*, 1981; Green and Brophy, 1982). The high rates of this cancer are surprising since few Chinese women smoke cigarettes (Deng and Gao, 1985). Furthermore, in Shanghai (Zheng and Gao, 1986) and elsewhere, hospital records have indicated that most of the lung tumors are adenocarcinomas, a type of lung cancer less strongly related to smoking (Lubin and Blot, 1984). To explore reasons for the high rates of lung cancer among women in Shanghai, the Shanghai Cancer Institute, in collaboration with the US National Cancer Institute, carried out a population-based case-control investigation. Herein we report the results of this study, quantifying the role of smoking and evaluating a variety of suspected risk factors.

MATERIAL AND METHODS

All newly diagnosed cases of primary lung cancer (9th Revision ICD 162) during the 2-year period February 1984–February 1986 among female residents of urban Shanghai aged 35–69 years were identified by a rapid reporting system for lung cancer established for this study. The system was built upon the existing Shanghai Cancer Registry, the oldest in China (Gao, 1982). Trained staff contacted medical facilities in Shanghai to ascertain new cases, so that interviews could be rapidly scheduled (typically within 2 weeks of diagnosis). The staff reviewed relevant medical records, abstracting data on the basis of diagnosis, histologic type, and the site of the tumor within the lung. Two senior pathologists and 4 senior clinicians were appointed to review the diagnostic information from all cases collected in the study, including X-ray films, cytologic and histologic slides.

Female controls were randomly selected within 5-year age strata from the general population of the Shanghai urban area. The number and age distribution of the controls were determined in advance from the number and age distribution of lung cancer cases reported to the Shanghai Cancer Registry during the period 1980–81. The selection procedure involved randomly choosing a neighborhood committee from among the approximately 1,300 committees in urban Shanghai, then randomly choosing a household group within the committee and ascertaining from existing rosters the names of all females in the appropriate age range. Among these persons, 2 were randomly selected. If the first was absent during the period of study or could not be interviewed, the second was accepted as a control. Tables of random numbers were used in the random sampling.

The cases and controls were interviewed by trained interviewers. A structured questionnaire was used to obtain information on demographic characteristics, exposure to tobacco, dietary and cooking practices, medical conditions, family history of lung cancer, menstrual and reproductive factors, job history and other variables. All completed questionnaires and medical abstracts were checked by a field supervisor, and the information was then abstracted on coding sheets for key-punching and computerization in the United States.

Statistical analyses of the collected data were based on multivariate techniques for case-control data (Breslow and Day, 1980). Logistic regression analyses were used to estimate summary relative risks (RR) of lung cancer associated with various factors, after adjusting for age (<55, 55–59, 60–64, 65–69), smoking (non-smoker; smoked less than 20 years or less than 10 cigarettes/day; smoked 20 or more years and 10–19 cigarettes/day; smoked 20 or more years and 20 or more cigarettes/day), education (no formal education, primary school, secondary school and higher) and other variables, and to evaluate statistical significance. Population attributable risk (PAR) estimates for smoking, adjusted for age, were also derived (Whittemore, 1983).

RESULTS

A total of 765 lung cancer patients were identified during the 2-year period and interviews conducted with 672 (88%). We excluded the 93 patients who died, including 38 ascertained by death certificate only. There were no patients who refused interview. Forty-three percent of the cases were diagnosed by tissue biopsy, 38% by cytology, and 19% by repeated

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TABLE I - RELATIVE RISKS OF LUNG CANCER ASSOCIATED WITH NUMBER OF CIGARETTES SMOKED PER DAY AND DURATION OF SMOKING

Number of cigarettes smoked per day	Duration of smoking							
	< 30 Years				> 30 Years			
	Cases	Controls	RR[1]	95% CI	Cases	Controls	RR	95% CI
< 10	36	45	1.4	0.9–2.2	34	29	2.4	1.4–4.1
10–19	19	11	2.6	1.2–5.7	56	33	3.2	2.0–5.1
20+	13	2	8.9	2.0–40.2	78	10	14.1	7.1–28.0

[1]Adjusted for age and education. Non-smokers are used as the reference group.

TABLE II - RELATIVE RISKS OF LUNG CANCER AMONG NON-SMOKING WOMEN ASSOCIATED WITH YEARS LIVED WITH A SMOKING HUSBAND

Years lived with smoking husband	Cases	Controls	RR[1]	95% CI
< 20	57	99	1.0	—
20–29	63	93	1.1	0.7–1.8
30–39	78	107	1.3	0.8–2.1
≥ 40	48	76	1.7	1.0–2.9

[1]Adjusted for age and education.

X-ray films. Among the 542 interviewed cases pathologically or cytologically diagnosed, adenocarcinoma was the predominant cell type accounting for 61% of all cases, 22% were squamous carcinomas, 6% were oat-cell (or small-cell undifferentiated) cancers, and 11% were mixtures and other cell types.

A total of 735 controls were interviewed. Among these 71 (9.7%) were "second" controls, chosen mainly because the first selected control had moved from the Shanghai urban area or was found to be outside the eligible age range. The distributions by age, education and marital status were generally similar between cases and controls. More controls than cases (32% *vs.* 20%), however, were in the oldest age group of 65–69 years, but all subsequent analyses were age-adjusted.

Cigarette smoking

Cigarette smoking was associated with a significantly increased risk of lung cancer, even though only 35% of the lung cancer patients (compared to 18% of the controls) had ever smoked. There was a 3.3-fold excess risk (95% CI = 2.5–4.2) of lung cancer among smokers, but risks were higher for squamous-cell carcinoma (RR = 7.2, 95% CI = 4.6–11.1) and oat-cell cancer (RR = 7.2, 95% CI = 3.6–17.0) than for adenocarcinoma (RR = 1.5, 95% CI = 1.0–2.1). The RR for all lung cancers combined tended to rise with increasing numbers of cigarettes smoked per day and with increasing duration of smoking (Table I). The excess reached 14-fold for females who smoked 20 or more cigarettes per day for more than 30 years. Similar trends existed for adenocarcinoma and for squamous/oat-cell cancers, but the magnitude of the increase was considerably greater for the latter (not shown).

We calculated population-attributable risk (PAR) estimates for smoking in each age group. The PAR rose with age, from 8% to 27% to 28% to 40% at ages < 55, 55–59, 60–64, and 65–69, respectively, primarily because the prevalence of smoking rose with age. In total, we estimated that 24% of all female lung cancers in Shanghai were due to smoking.

Passive smoking

No significant increase in risk was observed for overall exposure to environmental tobacco smoke during childhood (RR = 1.1, 95% CI = 0.7–1.7) or adult life (RR = 0.9, 95% CI = 0.6–1.4). For these calculations, exposure was said to occur if the subject had ever lived with a smoker. When exposure was defined in terms of husband's smoking, however, lung cancer risks among non-smoking women tended to increase with the number of years a woman lived with a husband who smoked, the RR reaching 1.7 among those with 40 or more compared to less than 20 years' exposure (Table II). The risk in this heavily exposed group was even higher (RR = 2.9, 95% CI = 1.0–8.9) for squamous- and oat-cell carcinoma.

Previous lung diseases

Since lung cancer in its early stages may be confused with other lung diseases, we excluded non-malignant lung diseases occurring within the 3 years preceding interview in evaluating the effect of prior lung disease upon lung cancer risk. Table III shows that previous tuberculosis, pneumonia and emphysema were significantly associated with lung cancer risk even after adjusting for smoking. Although some individuals reported having 2 or more of these diseases, the excesses for each persisted when those with multiple conditions were excluded. Further analysis (not shown) indicated that the effect of tuberculosis was not related to the use of isoniazid or streptomycin. While tuberculosis and pneumonia were related to both squamous/oat-cell carcinoma and adenocarcinoma of the lung, emphysema and chronic bronchitis were associated only with the squamous- and oat-cell types.

Cooking practices

Soybean and rapeseed oils were the oils used most often for cooking in Shanghai, with over 95% of women reporting the use of both products. Rapeseed oil, however, was reported as the most often used cooking oil by 52% of the cases compared to 45% of the controls. The overall increase in risk associated with rapeseed compared to soybean as the most often used oil was 1.4 (95% CI = 1.1–1.8). Table IV shows that the excess lung cancer risk associated with use of rapeseed oil existed at each level of reported frequency of eye irritation when cooking, a subjective variable representing severity of exposure to cooking vapors. The calculations for this Table excluded the few women who never cooked, and employed as the reference group women who most often used soybean oil but never or rarely reported eye irritation. Table IV also shows that risks of lung cancer were independently related to eye irritation, with the highest risks (RR = 2.8, 95% CI = 1.8–4.3) among those using rapeseed oil and frequently reporting irritation. The patterns were similar for squamous/oat-cell cancer and adenocarcinoma. We also observed, after adjusting for eye irritation, a 60% higher risk for lung cancer among women who reported considerable or somewhat smoky conditions in their homes when cooking, another rough measure of exposure to cooking vapors and to house ventilation (Table V). In addition, the risk ratios increased with the number of different dishes per week prepared by stir frying, deep frying, or boiling (Table VI). In contrast, no significant case/control differences were associated with the type of fuel used for cooking. The RR and 95% CI associated with coal, gas and wood as the usual fuels were 0.9 (0.7–1.3), 1.1 (0.7–1.5), and 1.0 (0.6–1.8) respectively. There was no trend in risk with increasing years of use of coal, the most common cooking fuel in Shang-

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TABLE III - RELATIVE RISKS OF LUNG CANCER ASSOCIATED WITH PREVIOUS LUNG DISEASES

Past lung diseases	Controls	All cases	RR[1]	95% CI	Squamous/oat-cell	RR[1]	95% CI	Adeno-carcinoma	RR[1]	95%
None	554	418	1.0	—	80	1.0	—	229	1.0	—
Tuberculosis	61	80	1.7	1.1-2.4	20	2.0	1.1-3.7	42	1.6	1.0-2.5
Pneumonia	35	65	1.9	1.2-3.0	16	1.8	0.9-3.8	26	1.5	0.9-2.7
Emphysema	18	37	2.0	1.0-3.7	19	4.5	2.0-10.3	6	0.7	0.3-2.0
Chronic bronchitis without emphysema	86	112	1.2	0.8-1.7	35	1.4	0.8-2.5	33	0.8	0.5-1.3
Others	30	30	1.3	0.7-2.2	8	1.7	0.7-4.2	13	1.0	0.5-2.0

[1]All risks adjusted for age, education and smoking and relative to women with no reported prior lung disease. Persons with more than one past lung disease are included in each lung disease category.

TABLE IV - RELATIVE RISKS OF LUNG CANCER ASSOCIATED WITH COOKING OIL USED MOST OFTEN AND FREQUENCY OF EYE IRRITATION WHEN COOKING

Eye irritation when cooking	Oil used most often	Cases	Controls	RR[1]	95% CI
Never or rarely	Soybean	140	214	1.0	—
	Rapeseed	145	193	1.2	0.9-1.7
Sometimes	Soybean	70	72	1.5	1.0-2.3
	Rapeseed	87	63	2.0	1.3-3.0
Frequently	Soybean	59	56	1.4	0.9-2.3
	Rapeseed	90	50	2.8	1.8-4.3
Total	Soybean	269	342	1.0	—
	Rapeseed	322	306	1.4	1.1-1.8

[1]Adjusted for age, education and smoking.

TABLE V - RELATIVE RISKS OF LUNG CANCER ASSOCIATED WITH FREQUENCY OF EYE IRRITATION AND HOUSE SMOKINESS WHEN COOKING

Eye irritation	House smokiness	Cases	Controls	RR[1]	95% CI
Never/rarely	None/slight	244	380	1.0	—
	Somewhat/considerable	55	55	1.6	1.0-2.5
Sometimes/frequently	None/slight	212	200	1.6	1.2-2.1
	Somewhat/considerable	109	60	2.6	1.8-3.7

[1]Adjusted for age, education and smoking.

TABLE VI - RELATIVE RISKS OF LUNG CANCER ASSOCIATED WITH NUMBER OF DIFFERENT DISHES PER WEEK PREPARED BY DIFFERENT METHODS OF COOKING

Number of dishes per week	Cases	Controls	RR[1]	95% CI
Stir frying				
≤20	336	408	1.0	—
20-24	198	211	1.2	0.9-1.5
25-29	48	47	1.2	0.8-1.9
≥30	34	15	2.6	1.3-5.0
Deep frying				
0	502	594	1.0	—
1	85	68	1.5	1.0-2.1
2	21	15	1.6	0.8-3.2
≥3	8	4	1.9	0.5-6.8
Boiling				
≤3	96	124	1.0	—
4-7	390	483	1.0	0.7-1.3
8-11	63	40	1.8	1.1-3.0
≥12	67	33	2.2	1.3-3.7

[1]Adjusted for age, education and smoking.

TABLE VII - RELATIVE RISKS OF LUNG CANCER ASSOCIATED WITH DIETARY INTAKE OF VITAMIN A

Vitamin exposure variable	Quartile level of consumption			
	I (High)	II	III	IV
Vitamin A index	1.0	0.6 (0.5-0.9)	0.8 (0.6-1.1)	0.5 (0.4-0.7)
Retinol-rich foods	1.0	0.9 (0.7-1.3)	1.0 (0.7-1.3)	0.9 (0.7-1.2)
Carotene-rich foods	1.0	0.6 (0.5-0.8)	0.5 (0.4-0.7)	0.5 (0.3-0.6)

[1]Risk relative to highest quartile of consumption and adjusted for age, education and smoking. 95% CI in parentheses.

hai. Exposures to coal or other fuel fumes were generally associated only with cooking, since nearly all homes in Shanghai were unheated.

Diet

The women were asked about their usual frequency of consumption during adulthood of 32 commonly eaten foods, including the major contributors of vitamin A. Using Chinese food composition tables to estimate the retinol and carotene content of each food and applying these estimates to its frequency of intake, an index of vitamin A consumption in retinol-equivalent units was constructed. The risks for lung cancer tended to be lower among those with low values of this index (Table VII). This association was accounted for mainly by a lower risk among those with a reduced consumption of carotene-rich foods (the dominant source being dark green vegetables). No effect on risk was found for consumption of the retinol-rich foods (mainly fish, eggs and liver). The patterns were generally similar for squamous/oat-cell cancer and adenocarcinoma, and for smokers and non-smokers.

Menstrual and reproductive factors

The risks of lung cancer were higher among women with shorter menstrual cycle lengths (Table VIII). The association was primarily seen for adenocarcinoma, which showed a strong dose-response relationship. Among women aged 55 years and over with a natural menopause, the risk of adenocarcinoma tended to increase with the total number of menstrual cycles over their lifetime. Some increased risk of adenocarcinoma was seen when natural menopause occurred at age 50 or later (RR = 1.3, 95% CI = 0.9-1.7, after adjusting for menstrual cycle length). No associations were seen with age at menarche, age at first pregnancy, or parity.

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TABLE VIII - RELATIVE RISKS OF LUNG CANCER ASSOCIATED WITH LENGTH OF MENSTRUAL CYCLE

Length of menstrual cycle (days)	All cases	Controls	RR[1]	95% CI	Squamous oat-cell	RR[1]	95% CI	Adeno-carcinoma	RR[1]	95% CI
>33	43	60	1.0	—	12	1.0	—	18	1.0	—
30–33	272	327	1.6	1.0–2.6	62	0.9	0.4–2.0	124	1.9	1.0–3.5
26–29	241	268	1.6	1.0–2.7	51	0.8	0.4–1.9	127	2.1	1.1–3.9
<26	98	78	2.2	1.3–3.7	23	1.6	0.7–3.9	54	2.9	1.5–5.7

[1]Adjusted for age, education, smoking and regularity of menstruation.

TABLE IX - RELATIVE RISKS OF LUNG CANCER FOR WOMEN EVER EMPLOYED IN MAJOR OCCUPATIONAL GROUPS

	Occupation category[1]	Cases	Controls	RR[2]	95% CI
I–II	Professionals and technicians; leaders of state organizations, party and mass organizations and enterprise units	113	116	1.0	0.7–1.4
III–IV	Office and related personnel; sales workers	75	96	0.7	0.5–1.0
V	Service workers	159	160	1.0	0.8–1.4
VI	Agricultural, forestry, animal husbandry and fishery workers	24	21	1.1	0.6–2.1
VII–IX	Production, transportation and other related workers	436	471	1.1	0.9–1.4
0	Never worked	61	75	1.1	0.7–1.6

[1]Women employed in more than one occupational category are included in each category in which they worked. The coding scheme was based on the system used in the 1982 Population Census of the People's Republic of China (Population Census Office, 1985). [2]Adjusted for age, education and smoking.

Occupation

Most women reported working outside the home, but case/control differences according to major occupational categories were small (Table IX). No major occupations were associated with increased risk of lung cancer. A decreased risk, however, was observed for women ever employed in the cotton textile industry, the largest employer of women in Shanghai. There was a slight increase in the relative risk of lung cancer among women ever employed as cooks (RR = 1.2, 95% CI = 0.6–2.1), but few worked longer than 20 years.

Family history

The cancer patients reported about the same frequency of lung cancer in their mothers (1.0%) and fathers (1.7%) as the controls (1.0% and 1.5%, respectively). The RR, adjusted for age, education and smoking, associated with having a parent with lung cancer was 1.1 (95% CI = 0.6–2.3). More sibs were reported to have lung cancer, but the numbers affected were small (6 cases, 3 controls; RR = 3.0, 95% CI = 0.7–12.5). Only one child, of a control, had lung cancer.

DISCUSSION

The high incidence of lung cancer among women in Shanghai, together with the low prevalence of smoking in the general population, led us to consider a number of possible etiologic factors. **While cigarette smoking was an important cause of lung cancer, showing a clear dose-response trend,** the majority of lung tumors, particularly adenocarcinomas, occurred among non-smokers.

Environmental tobacco smoke may account for some, but probably few, of the cancers among non-smokers, since there was little or no association with ever having lived with a smoker. Among non-smoking women married to smokers, however, there was an upward trend in risk associated with increasing years of exposure. This latter finding is consistent with reports in other parts of the world. When data from nearly a dozen studies evaluating passive smoking were combined (Blot and Fraumeni, 1986), an overall 30% excess of lung cancer (RR = 1.3, 95% CI = 1.1–1.5) was found among non-smoking women married to smokers, with the RR reaching 1.7 among those most heavily exposed.

Although the causal significance of the relation of prior lung disease to lung cancer remains to be clarified, the high prevalence of previous pulmonary infections may have contributed in part to the high incidence of lung cancer among Shanghai women. Earlier in this century, non-malignant lung disease was one of the leading causes of death in China (Kan, 1981). With the advent of antibiotics and improved living conditions, the incidence and mortality of chronic lung diseases, particularly tuberculosis, declined. Nevertheless, a substantial portion (38%) of the women with lung cancer in this study reported prior lung disease, including 12% who were long-term survivors of tuberculosis, whereas significantly lower percentages of controls reported these diseases. To some extent it is possible that recall or ascertainment bias may contribute to the associations observed with prior lung diseases. The elevated risk of lung cancer following tuberculosis, however, is consistent with recent studies in other countries, and is not explained by cigarette smoking or treatment with isoniazid, a pulmonary carcinogen in laboratory animals (Howe *et al.*, 1979; Hinds *et al.*, 1982; Bakris *et al.*, 1983).

Emphysema was also significantly related to lung cancer, after adjustment for smoking habits, with the excess limited to squamous- and oat-cell carcinomas. This finding adds to the evidence that chronic obstructive pulmonary disease enhances the risk of lung cancer (Skillrud *et al.*, 1986), even when controlling for smoking practices. Also noteworthy is the elevated risk associated with prior pneumonia, especially since an association with lung adenocarcinoma has previously been reported among women in Los Angeles (Wu *et al.*, 1985). While pneumonia typically occurred during adulthood in our study, the finding in Los Angeles primarily concerned childhood infection.

Little evidence was found to implicate the type of fuels used for cooking in lung cancer risk, consistent with findings from

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Hong Kong (Koo *et al.*, 1983). The risks of lung cancer among Shanghai women increased, however, with various measures of exposure to cooking oil vapors. These included the number of different dishes prepared per week by either stir frying, deep frying, or boiling, the frequency of eye irritation when cooking, and the smokiness of the house when cooking. In Chinese wok cooking, regardless of the method used, oil is usually poured into a wok and heated to high temperatures before meat or vegetables are added. Even boiling may entail some exposure to cooking oil vapors, since oil is often added to the water before heating. Consequently, the living quarters may become smoky during cooking, with opportunity for exposure to inhalable cooking oil vapors.

The plausibility of the hypothesis that lung cancer may be related to cooking oil vapors, particularly from rapeseed oils used in Shanghai, is enhanced by recent experimental investigations. In one study the mutagenicity of products from cooking oil was assayed by the Ames test (Qu *et al.*, 1986). The extracts of condensed volatiles of rapeseed oil, refined rapeseed oil, and soybean oil heated at about 270°C were all positive in tester strain TA98 activated with S9. The mutagenicity of the extract from rapeseed oil volatiles was stronger than that from soybean oil volatiles. There was no evidence of mutagenicity in the oils themselves, either heated or unheated. In another study, the extracts of condensed volatiles of rapeseed oil enhanced the yield of micronuclei in polychromatic erythrocytes of the bone marrow of mice, with a clear dose-response relationship, reflecting damage of chromosomes and cell genotoxicity by rapeseed oil volatiles (Chen, 1987). Although these tests often correlate with carcinogenic potential, no bioassay studies have yet been carried out, to our knowledge. If the effect of rapeseed oil smoke on lung cancer incidence is real, the problem is of great importance to populations of eastern central China and other areas of the world where the oil is often used for cooking. Chinese rapeseed oil, which is pressed from seeds of *Brassica campestris*, contains about 50% erucic acid (Chinese Academy of Medical Sciences, 1981), in contrast to rapeseed oil with <2% erucic acid (Canbra oil), which was recently approved for sale in the United States (Federal Register, 1985).

Several studies have shown that the risk of lung cancer is elevated by a low intake of foods containing vitamin A, particularly as its precursor beta-carotene (Colditz *et al.*, 1987). Although reported mainly in Western countries, this association has also been noted among Chinese women in Singapore (MacLennan *et al.*, 1977). However, we found no evidence of a protective effect among women in Shanghai, where intake of fresh, carotene-rich, dark green vegetables is high by world standards. In fact, a positive association was observed between carotene intake and lung cancer risk in females (in contrast to no association in males). We have no ready explanation for this unusual finding in females, which was observed also in a case-control study of lung cancer in Hawaii (Hinds *et al.*, 1984). However, the protective effect of carotene-rich foods was mainly confined to current smokers in one large-scale study (Ziegler *et al.*, 1986), and thus the effect may be less evident in Shanghai where few women smoke.

A clue to hormonal factors was suggested by an association between menstrual cycle length and lung adenocarcinoma. A 3-fold difference in adenocarcinoma risk was found among Shanghai women reporting short (<26 days) compared to long (>33 days) menstrual cycles, with only a weak trend for squamous- and oat-cell cancers. A relation of short menstrual cycles to breast cancer risk has been suggested in data from Sweden (Olsson *et al.*, 1983) and, to a lesser extent, the United States (Sherman *et al.*, 1982). Some increases in lung adenocarcinoma risk were also associated with late menopause and with a high estimated total number of menstrual cycles among women aged 55 and over having a natural menopause. A role of hormonal factors is also suggested by the observation that among non-smokers adenocarcinoma affects proportionately more females than males (Lubin and Blot, 1984), and by the findings of estrogen and progesterone receptors in some lung adenocarcinomas of women (Chaudhuri *et al.*, 1982). We discovered no relation to oral contraceptives or replacement estrogen therapy, but use of these compounds among women in the study group was rare in Shanghai. It seems unlikely that the menstrual patterns of Chinese women contribute greatly to their high lung cancer risk, but the internal consistency of the trends suggests that future studies of lung cancer in China and elsewhere should examine endocrine hypotheses in more detail.

This large population-based case-control study of lung cancer in urban Shanghai has confirmed that cigarette smoking is a strong risk factor among Chinese women, but only accounts for about one-fourth of all newly diagnosed cases. Causes of the remainder are unclear, but occupational factors did not appear to be important, nor did familial tendency to lung cancer. Our data suggest, however, that prior lung diseases, hormonal factors, and cooking practices may be involved. Most provocative are the associations with cooking oil volatiles, and further investigations are needed to evaluate their contribution to the high lung cancer rates among Chinese women in various parts of the world.

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